10758917

=> d his

(FILE 'HOME' ENTERED AT 13:08:46 ON 11 MAR 2004)

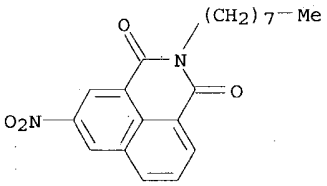
FILE 'REGISTRY' ENTERED AT 13:08:55 ON 11 MAR 2004
L1 1 S 207107-72-0/RN
L2 1 S 207107-67-3/RN

=> d l2 all

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **207107-67-3** REGISTRY
ED Entered STN: 14 Jun 1998
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-nitro-2-octyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H22 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C5N-C6-C6	NC5-C6-C6	6-6-6	C12N	1784.14.8	1



Calculated Properties (CALC)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	44255	pH 1	(1) ACD
Bioconc. Factor (BCF)	44272	pH 4	(1) ACD
Bioconc. Factor (BCF)	44272	pH 7	(1) ACD
Bioconc. Factor (BCF)	44272	pH 8	(1) ACD
Bioconc. Factor (BCF)	44272	pH 10	(1) ACD
Boiling Point (BP)	521.9+/-33.0 deg C	760.0 Torr	(1) ACD
Enthalpy of Vap. (HVAP)	79.53+/-3.0 kJ/mol		(1) ACD
Flash Point (FP)	269.5+/-45.7 deg C		(1) ACD
H acceptors (HAC)	6		(1) ACD
H donors (HD)	0		(1) ACD
Koc (KOC)	73594	pH 1	(1) ACD
Koc (KOC)	73621	pH 4	(1) ACD
Koc (KOC)	73621	pH 7	(1) ACD
Koc (KOC)	73621	pH 8	(1) ACD
Koc (KOC)	73621	pH 10	(1) ACD
logD (LOGD)	6.42	pH 1	(1) ACD
logD (LOGD)	6.42	pH 4	(1) ACD
logD (LOGD)	6.42	pH 7	(1) ACD
logD (LOGD)	6.42	pH 8	(1) ACD
logD (LOGD)	6.42	pH 10	(1) ACD
logP (LOGP)	6.417+/-0.270		(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 1	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 4	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 7	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 8	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 10	(1) ACD
Molecular Weight (MW)	354.40		(1) ACD
Vapor Pressure (VP)	5.43E-11 Torr	25.0 deg C	(1) ACD

10758917

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software
Solaris V4.67 ((C) 1994-2004 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

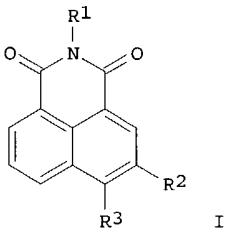
REFERENCE 1

AN 128:317269 CA
TI Benzoisoquinolinedione neurotrophin antagonist compositions and therapeutic use
IN Tehim, Ashok; Chen, Xiannong
PA Allelix Biopharmaceuticals Inc., Can.; Tehim, Ashok; Chen, Xiannong
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-47
ICS C07D221-14; C07D401-04; C07D401-06
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817278	A1	19980430	WO 1997-CA779	19971020
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9746968	A1	19980515	AU 1997-46968	19971020
	AU 728523	B2	20010111		
	EP 930883	A1	19990728	EP 1997-909098	19971020
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 335291	A	20010223	NZ 1997-335291	19971020
	JP 2001503397	T2	20010313	JP 1998-518756	19971020
	BR 9712424	A	20011120	BR 1997-12424	19971020
	MX 9903637	A	20000531	MX 1999-3637	19990420
	US 2002169182	A1	20021114	US 2001-758917	20010111

PRAI	GB 1996-21902	19961021
	GB 1997-10904	19970527
	WO 1997-CA779	19971020
	US 1999-292458	19990415
	US 1999-440505	19991115
	US 2000-592015	20000612

GI



I

AB Pharmaceutical compns. comprising I (R1 = alkyl, aryl-lower alkyl, heterocyclyl-lower alkyl, etc.; R2, R3 = H, NO2, halo, di(lower alkyl)amino, cyano, etc.), or pharmaceutically acceptable salts or certain in vivo hydrolyzable esters or amides thereof, in an amount effective to inhibit neurotrophin-mediated activity, and a suitable carrier, are described. The compns. are useful for inhibiting undesirable neurotrophin-mediated activity, e.g. the neurite outgrowth that occurs in some neurodegenerative disease states. N-[5-nitro-1H-benz[de]isoquinoline-

10758917

1,3(2H)-dione]-2-aminoethanol (II) was prepared from 3-nitro-1,8-naphthalic anhydride and 2-hydroxyethylhydrazine. II was tested for ability to inhibit neurite outgrowth, as well as in an animal model of neuropathic pain. Compds. of the invention were also tested for ability to inhibit NGF binding to P75 and TrkA.

ST benzoisoquinolinedione neurotrophin antagonist neurite outgrowth inhibition; neurodegenerative disease benzoisoquinolinedione neurotrophin antagonist prepn; neuropathic pain benzoisoquinolinedione neurotrophin antagonist

IT Neurotrophic factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(TrkA; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
Pain
Skin, disease
Skin, disease
(allodynia, tactile; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Analgesics
Drug delivery systems
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(brain-derived; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
(hyperalgesia, thermal; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Nerve
(neuron; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
(neuropathic; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Axon
(outgrowth, inhibition; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Nerve growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p75; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 9061-61-4, NGF
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 79070-65-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 2382-08-3 5450-40-8 5690-46-0 5690-46-0D, esters and amides 5810-79-7 6917-30-2D, esters and amides 15965-03-4 15965-03-4D, esters and amides 51411-04-2D, esters and amides 53497-34-0 53497-34-0D, esters and amides 66266-36-2 69408-78-2 74240-33-8 79070-65-8D, esters and amides 94887-57-7 100873-54-9 130001-49-9 162265-47-6 194610-48-5 206982-84-5 207107-62-8 207107-63-9 207107-64-0 207107-65-1 207107-66-2 207107-67-3 207107-68-4 207107-69-5 207107-70-8 207107-71-9 207107-72-0 207107-73-1 207107-74-2 207107-75-3 207107-76-4 207107-77-5 207107-78-6 207107-79-7 207107-80-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic

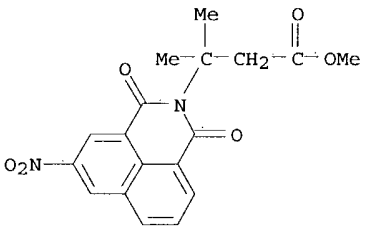
use)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Arient, J; COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS 1961, V26, P2774 CAPLUS
(2) Brana, M; EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY CHIMICA THERAPEUTICA 1981, V16(3), P207 CAPLUS
(3) Brana, M; JOURNAL OF ORGANIC CHEMISTRY 1996, V61(4), P1369 CAPLUS
(4) I P A International Pharmaceutical Associated; EP 0206322 A 1986 CAPLUS
(5) Kievsky Institut Endokrinologii; FR 2521139 A 1983 CAPLUS
(6) Knoll Ag; DE 3707652 A 1988 CAPLUS
(7) Laboratorios Made S A; DE 2323555 A 1974 CAPLUS
(8) Sestanj, K; US 3821383 A 1974 CAPLUS
(9) Sestanj, K; US 4254109 A 1981 CAPLUS
(10) Shunichiro, N; NIPPON KAGAKU ZASSHI 1965, V86(7), P696

=> d l1 all

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **207107-72-0** REGISTRY
ED Entered STN: 14 Jun 1998
CN 1H-Benz[de]isoquinoline-2(3H)-propanoic acid, β,β-dimethyl-5-nitro-1,3-dioxo-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H16 N2 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C5N-C6-C6	NC5-C6-C6	6-6-6	C12N	1784.14.8	1



Calculated Properties (CALC)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	358	pH 1	(1) ACD
Bioconc. Factor (BCF)	358	pH 4	(1) ACD
Bioconc. Factor (BCF)	358	pH 7	(1) ACD
Bioconc. Factor (BCF)	358	pH 8	(1) ACD
Bioconc. Factor (BCF)	358	pH 10	(1) ACD
Boiling Point (BP)	537.9+/-35.0 deg C	760.0 Torr	(1) ACD
Enthalpy of Vap. (HVAP)	81.49+/-3.0 kJ/mol		(1) ACD
Flash Point (FP)	279.1+/-46.7 deg C		(1) ACD
H acceptors (HAC)	8		(1) ACD
H donors (HD)	0		(1) ACD
Koc (KOC)	2338	pH 1	(1) ACD
Koc (KOC)	2339	pH 4	(1) ACD
Koc (KOC)	2339	pH 7	(1) ACD
Koc (KOC)	2339	pH 8	(1) ACD
Koc (KOC)	2339	pH 10	(1) ACD
logD (LOGD)	3.66	pH 1	(1) ACD
logD (LOGD)	3.66	pH 4	(1) ACD
logD (LOGD)	3.66	pH 7	(1) ACD
logD (LOGD)	3.66	pH 8	(1) ACD

10758917

logD (LOGD)	3.66	pH 10	(1) ACD
logP (LOGP)	3.663+/-0.330		(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 1	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 4	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 7	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 8	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 10	(1) ACD
Molecular Weight (MW)	356.33		(1) ACD
Vapor Pressure (VP)	1.22E-11 Torr	25.0 deg C	(1) ACD

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software Solaris V4.67 ((C) 1994-2004 ACD/Labs)

See HELP PROPERTIES for information about property data sources in REGISTRY.

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

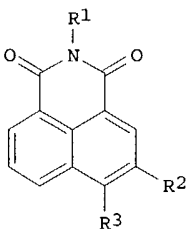
REFERENCE 1

AN 128:317269 CA
TI Benzoisoquinolinedione neurotrophin antagonist compositions and therapeutic use
IN Tehim, Ashok; Chen, Xiannong
PA Allelix Biopharmaceuticals Inc., Can.; Tehim, Ashok; Chen, Xiannong
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-47
ICS C07D221-14; C07D401-04; C07D401-06
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817278	A1	19980430	WO 1997-CA779	19971020
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9746968	A1	19980515	AU 1997-46968	19971020
	AU 728523	B2	20010111		
	EP 930883	A1	19990728	EP 1997-909098	19971020
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 335291	A	20010223	NZ 1997-335291	19971020
	JP 2001503397	T2	20010313	JP 1998-518756	19971020
	BR 9712424	A	20011120	BR 1997-12424	19971020
	MX 9903637	A	20000531	MX 1999-3637	19990420
	US 2002169182	A1	20021114	US 2001-758917	20010111

PRAI	GB 1996-21902	19961021
	GB 1997-10904	19970527
	WO 1997-CA779	19971020
	US 1999-292458	19990415
	US 1999-440505	19991115
	US 2000-592015	20000612

GI



I

AB Pharmaceutical compns. comprising I (R1 = alkyl, aryl-lower alkyl, heterocyclyl-lower alkyl, etc.; R2, R3 = H, NO2, halo, di(lower alkyl)amino, cyano, etc.), or pharmaceutically acceptable salts or certain in vivo hydrolyzable esters or amides thereof, in an amount effective to inhibit neurotrophin-mediated activity, and a suitable carrier, are described. The compns. are useful for inhibiting undesirable neurotrophin-mediated activity, e.g. the neurite outgrowth that occurs in some neurodegenerative disease states. N-[5-nitro-1H-benz[de]isoquinoline-1,3(2H)-dione]-2-aminoethanol (II) was prepared from 3-nitro-1,8-naphthalic anhydride and 2-hydroxyethylhydrazine. II was tested for ability to inhibit neurite outgrowth, as well as in an animal model of neuropathic pain. Compds. of the invention were also tested for ability to inhibit NGF binding to P75 and TrkA.

ST benzoisoquinolinedione neurotrophin antagonist neurite outgrowth inhibition; neurodegenerative disease benzoisoquinolinedione neurotrophin antagonist prepn; neuropathic pain benzoisoquinolinedione neurotrophin antagonist

IT Neurotrophic factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(TrkA; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
Pain
Skin, disease
Skin, disease
(allodynia, tactile; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Analgesics
Drug delivery systems
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(brain-derived; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
(hyperalgesia, thermal; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Nerve
(neuron; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Pain
(neuropathic; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Axon
(outgrowth, inhibition; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT Nerve growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p75; benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 9061-61-4, NGF
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 79070-65-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

IT 2382-08-3 5450-40-8 5690-46-0 5690-46-0D, esters and amides 5810-79-7 6917-30-2D, esters and amides 15965-03-4 15965-03-4D, esters and amides 51411-04-2D, esters and amides 53497-34-0 53497-34-0D, esters and amides 66266-36-2 69408-78-2 74240-33-8

79070-65-8D, esters and amides 94887-57-7 100873-54-9 130001-49-9
162265-47-6 194610-48-5 206982-84-5 207107-62-8 207107-63-9
207107-64-0 207107-65-1 207107-66-2 207107-67-3 207107-68-4
207107-69-5 207107-70-8 207107-71-9 207107-72-0 207107-73-1
207107-74-2 207107-75-3 207107-76-4 207107-77-5 207107-78-6
207107-79-7 207107-80-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoisoquinolinedione neurotrophin antagonist compns. and therapeutic use)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Arient, J; COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS 1961, V26, P2774 CAPLUS
(2) Brana, M; EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY CHIMICA THERAPEUTICA 1981, V16(3), P207 CAPLUS
(3) Brana, M; JOURNAL OF ORGANIC CHEMISTRY 1996, V61(4), P1369 CAPLUS
(4) I P A International Pharmaceutical Associated; EP 0206322 A 1986 CAPLUS
(5) Kievsky Institut Endokrinologii; FR 2521139 A 1983 CAPLUS
(6) Knoll Ag; DE 3707652 A 1988 CAPLUS
(7) Laboratorios Made S A; DE 2323555 A 1974 CAPLUS
(8) Sestanj, K; US 3821383 A 1974 CAPLUS
(9) Sestanj, K; US 4254109 A 1981 CAPLUS
(10) Shunichiro, N; NIPPON KAGAKU ZASSHI 1965, V86(7), P696